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## **THE PATENTS ACT, 1952, AS AMENDED.**

**APPLICATION FOR A PATENT UNDER INTERNATIONAL ARRANGEMENTS**

**(WITH AUTHORISATION F AGENT)**

**Filing date and Application No.**

631802

of Applicant(s): MERCK & CO., Inc.

**Address(es) of applicant(s) :** 126 East Lincoln Avenue  
Rahway, New Jersey  
United States of America

**Full name(s) of inventor(s):**

MARcia ELIZABETH CHRISTY

I/We do hereby declare that I am/we are in possession of an invention the title of which is

"5,10-METHANO DERIVATIVES OF 10,11-DIHYDRODIBENZOCYCLOHEPTENES AND PROCESSES"

I am/We are the assignee(s)/legal representative(s) of the inventor(s). Application(s) for protection for the invention has/have been made in the following country/countries and on the following official dates i.e.:—

1. (country) United States of America (date) 21 March 1967 (number) 624,705  
2. (country) (date) (number)  
3. (country) (date) (number)

The said application or each of the said applications was the first application in a convention country in respect of the relevant invention by me/us or by any person from whom I/we derive title. To the best of my/our knowledge and belief there is no lawful ground for objection to the grant of a patent to me/us on this application. I/We pray that a patent be granted to me/us for the invention in priority over other applicants and that such patent shall have the official date of the first application in a convention country i.e. 21 March 1967.

I/We hereby appoint the partners and qualified staff of the firm of D. M. KISCH & Co., jointly and severally, to act for me/us in all matters relating to this application and any letters patent granted thereon.

Dated this 7<sup>th</sup> day of February 1968

**Address for service:**

D. M. KISCH & CO.,

CORPORATION BUILDING,  
COMMISSIONER STREET,  
JOHANNESBURG.

MERCK & CO., Inc.

| Table of Classification |           |
|-------------------------|-----------|
| Class                   | Sub-class |
|                         |           |

*Stephen G. Zelenzak*  
Stephen G. Zelenzak  
Administrative Assistant-Patents

**Signature of Applicant/s and Capacity**

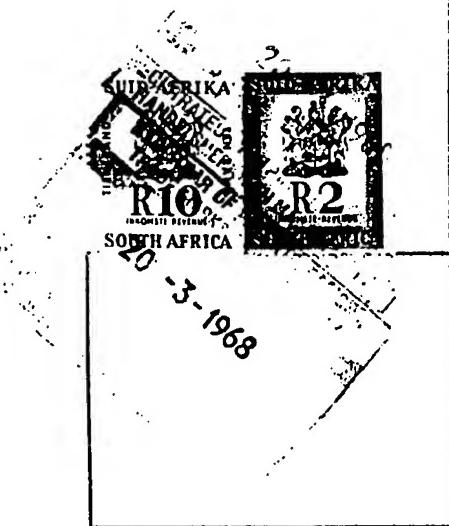
REPUBLIC OF SOUTH AFRICA

THE PATENTS ACT, 1952, AS AMENDED

COMPLETE SPECIFICATION

Filing date and Application No.

68/1802



Full name(s) of Applicant(s): MERCK & CO., INC.

Address(es) of Applicant(s): 126 East Lincoln Avenue, Rahway, New Jersey,  
United States of America

Title of Invention: "5,10-METHANO DERIVATIVES OF 10,11-DIHYDRODIBENZOCYCLOCHEPTENES AND PROCESSES"

I/We do hereby declare this invention, the manner in which and the method by which it is to be performed, to be particularly described and ascertained in and by the following statement:—

*[Signature]*

1           This invention relates to 10,11-dihydro-5,10-  
2 methano derivatives of dibenzocycloheptenes having the 5-  
3 position substituted by an organic radical and, particularly,  
4 the invention relates to 10,11-dihydro-5,10-methanodibenzo-  
5 cycloheptenes having a saturated or unsaturated alkyl sub-  
6 stituent or a saturated or unsaturated substituted-alkyl  
7 substituent attached to the 5-position.

8           The invention includes 10,11-dihydro-5,10-methano-  
9 dibenzocycloheptenes having a 5-position aminoalkyl side  
10 chain optionally further substituted by ketonic oxygen,  
11 hydroxyl and, in addition, is saturated or unsaturated.

12           The invention also includes 5-alkanoyl-10,11-di-  
13 hydro-5H-dibenzo[a,d]cycloheptene compounds which are inter-  
14 mediates in the preparation of the biologically-active  
15 compounds of my invention.

16           The invention also relates to methods of preparing  
17 5-aminoalkyl-10,11-dihydro-5,10-methanodibenzocycloheptene  
18 compounds and to intermediates in the preparation of said  
19 compounds from 9-alcanoyl, e.g., 9-acetylanthracene compounds  
20 such as 9-alcanoyl-9,10-dihydro-9,10-ethano-11-(carboxy or  
21 carbalkoxy)anthracene compounds, 5-alcanoyl-10,11-dihydro-  
22 5,10-methano-11-(acyloxy or hydroxy)dibenzocycloheptene  
23 compounds.

24           The new compounds representative of my invention  
25 are 5,10-methano-10,11-dihydrodibenzoheptene compounds  
26 which contain alkyl, alkanoyl or alkanoyloxy substituents at  
27 the 5-position of the dibenzocycloheptene molecule. Repre-  
28 sentative groups of compounds included within the scope of  
29 my invention are those in which the 5-alkyl substituent is  
30 substituted at any of the carbon atoms of the side chain

1 with a primary amine, a secondary amine, or a tertiary amine  
2 substituent, particularly, N-alkylated secondary or tertiary  
3 amine groups wherein the N-alkyl radicals are methyl, ethyl,  
4 propyl, isopropyl, butyl, secondary butyl, isobutyl and  
5 t-butyl substituents.

6 There are also included tertiary aminoalkyl-  
7 substituted compounds in which the tertiary amine nitrogen is  
8 linked in a heterocyclic ring containing 5 or 6 members which  
9 optionally contains additional hetero atoms such as nitrogen,  
10 oxygen or sulphur linked with the requisite number of carbons  
11 to complete the 5- or 6-membered heterocyclic ring.

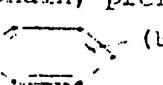
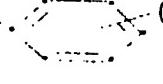
12 Also included within the scope of my invention are  
13 compounds which contain additional functional substituents  
14 attached to any of the carbons of the alkyl side chain.  
15 These substituents include hydroxyl, ketonic oxygen, acyloxy,  
16 (particularly alkanoyloxy), halo and/or amino (primary,  
17 secondary or tertiary amino including heterocyclic amino of  
18 the type mentioned hereinabove).

19 The compounds of my invention include 5-alkyl or  
20 substituted-alkyl 5,10-methano-10,11-dihydrodibenzocyclo-  
21 heptene compounds wherein the 5-alkyl or substituted-alkyl  
22 radicals include both saturated and unsaturated derivatives  
23 including 5-methyl, ethyl, propyl, isopropyl, butyl, branched-  
24 chain butyl such as isobutyl, secondary butyl and t-butyl as  
25 well as pentyl and hexyl, and the corresponding unsaturated  
26 derivatives such as 5-vinyl, propenyl, isopropenyl, butenyl,  
27 pentenyl and hexenyl 5,10-methano-10,11-dihydrodibenzocyclo-  
28 heptenes, especially including those compounds wherein the  
29 double bond of the unsaturated side chain at the 5-position  
30 is attached to the carbon linking the unsaturated side chain

1 to the dibenzocycloheptene nucleus, e.g., 5-(1-propenyl)-  
2 5,10-methano-10,11-dihydrodibenzocycloheptene.  
3 Especially preferred compounds of my invention  
4 are 5-substituted 5,10-methano-10,11-dihydrodibenzocyclo-  
5 heptene compounds wherein the substituent attached to the  
6 5-position is an aminoalkyl substituent, an alkylaminoalkyl  
7 substituent, a dialkylaminoalkyl substituent or a hetero-  
8 cyclicaminoalkyl substituent. Such compounds include  
9 5-(aminoalkyl)-5,10-methano-10,11-dihydrodibenzocycloheptene,  
10 5-(N-alkylaminoalkyl)-5,10-methano-10,11-dihydrodibenzocyclo-  
11 heptene, 5-(N,N-dialkylaminoalkyl)-5,10-methano-10,11-dihydro-  
12 dibenzocycloheptene, and 5-(heterocyclicaminoalkyl)-5,10-  
13 methano-10,11-dihydrodibenzocycloheptene. The alkyl side  
14 chain through which the aminoalkylamino or heterocyclic amino  
15 substituent is linked to the dibenzocycloheptene nucleus at  
16 the 5-position is optionally a straight or branched-chain  
17 alkyl substituent, preferably of from 1 to 6 carbon atoms as,  
18 for example, methyl, ethyl, propyl, isopropyl, butyl or  
19 branched-chain butyl, pentyl or hexyl or branched-chain  
20 pentyl or hexyl radicals.

21 In addition to the above-mentioned 5,10-methano-  
22 dibenzocycloheptene compounds, the intermediate 9,10-ethano-  
23 9,10-dihydroanthracene compounds form part of my invention.  
24 These intermediate compounds are prepared by heating a  
25 9-alkanoylanthracene compound with acrylic acid or a function-  
26 ally equivalent derivative thereof such as an acrylic acid  
27 ester, acrylonitrile, or the like, to produce the desired  
28 9-alkanoyl-9,10-ethano-9,10-dihydroanthracene-11-carboxylic  
29 acid (alkyl carboxylate or nitrile).

30 The new compounds of my invention, including the

1 intermediate compounds as well as the pharmaceutically-  
2 active end products, also include substituents at the 11-  
3 position. The substituents are selected from the group con-  
4 sisting of H, OH, OY, =NOR°, =NOY, NH<sub>2</sub>, NHSO<sub>2</sub>R, N<sup>R°</sup><sub>R'''</sub> =NNH<sub>2</sub>  
5 and, in the case wherein the substituent is OH or OY, there  
6 can be an alkyl group as defined by R''' replacing the hydrogen  
7 at the 11-position; wherein R is lower alkyl, straight or  
8 branched-chain, preferably having up to 6 carbon atoms,  
9 -(CH<sub>2</sub>)<sub>n</sub>- (B)<sub>n</sub> wherein B is hydrogen, halogen, tri-  
10 fluoromethyl, lower alkyl, straight or branched-chain,  
11 preferably having up to 4 carbon atoms, lower alkoxy, straight  
12 or branched-chain, preferably having up to 4 carbon atoms,  
13 and n represents a whole number of from 0 to 3; R° is  
14 hydrogen or lower alkyl, straight or branched chain, prefer-  
15 ably having up to 6 carbon atoms, R''' is lower alkyl, straight  
16 or branched chain, preferably having up to 6 carbon atoms;  
17 Y is alkanoyl, straight or branched-chain, preferably having  
18 up to 18 carbon atoms and may contain unsaturation,  
19 -C<sup>0</sup>-(CH<sub>2</sub>)<sub>n</sub>- (B)<sub>n</sub> wherein B and n are as defined  
20 above.

21 Representative compounds encompassed within the  
22 scope of the present invention include:

- 23 10,11-dihydro-5,10-methano-11-hydroxy-5-[3-(1-piperidyl)-  
24 propyl]-5H-dibenzo[a,d]cycloheptene,  
25 10,11-dihydro-5,10-methano-11-hydroxy-5-[3-(1-methyl-4-  
26 piperazinyl)propyl]-5H-dibenzo[a,d]cycloheptene.  
27 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-dimethylaminopropyl)-  
28 5H-dibenzo[a,d]cycloheptene,  
29 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-methylaminopropyl)-  
30 5H-dibenzo[a,d]cycloheptene,  
31 7-chloro-10,11-dihydro-5,10-methano-11-hydroxy-5-(3-dimethyl-  
32 aminopropyl)-5H-dibenzo[a,d]cycloheptene,

- 1 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-hydroxyimino-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene,
- 2 11-methylamino-10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-5H-dibenzo[a,d]cycloheptene,
- 3 11-diethylamino-10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-5H-dibenzo[a,d]cycloheptene,
- 4 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-ethyl-11-hydroxy-5H-dibenzo[a,d]cycloheptene,
- 5 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-methylaminopropyl)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene,
- 6 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-dimethylaminopropyl)-3-trifluoromethyl-5H-dibenzo[a,d]cycloheptene,
- 7 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-diethylamino-propyl)-3-dimethylsulfamoyl-5H-dibenzo[a,d]cycloheptene,
- 8 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-dimethylaminopropyl)-5H-dibenzo[a,d]cycloheptene,
- 9 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-dimethylaminopropyl)-3-trifluoromethyl-5H-dibenzo[a,d]cycloheptene,
- 10 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-diethylamino-propyl)-3-dimethylsulfamoyl-5H-dibenzo[a,d]cycloheptene,
- 11 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-dimethylamino-propyl)-3-dimethylsulfamoyl-5H-dibenzo[a,d]cycloheptene,
- 12 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-diethylamino-propyl)-3-dimethylsulfamoyl-5H-dibenzo[a,d]cycloheptene,
- 13 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-diethylamino-propyl)-3-dimethylsulfamoyl-5H-dibenzo[a,d]cycloheptene,
- 14 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-dimethylaminopropyl)-5H-dibenzo[a,d]cycloheptene,
- 15 10,11-dihydro-5,10-methano-5-(3-dimethylaminopropyl)-5H-dibenzo[a,d]cycloheptene,
- 16 10,11-dihydro-5,10-methano-5-(3-dimethylaminopropyl)-5H-dibenzo[a,d]cycloheptene,
- 17 10,11-dihydro-5,10-methano-5-(3-methylaminopropyl)-5H-dibenzo[a,d]cycloheptene,
- 18 10,11-dihydro-5,10-methano-5-(3-methylaminopropyl)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene,
- 19 10,11-dihydro-5,10-methano-5-(3-methylaminopropyl)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene,
- 20 10,11-dihydro-5,10-methano-5-(3-dimethylaminopropyl)-3-trifluoromethyl-5H-dibenzo[a,d]cycloheptene,
- 21 10,11-dihydro-5,10-methano-5-(3-dimethylaminopropyl)-3-dimethylsulfamoyl-5H-dibenzo[a,d]cycloheptene,
- 22 10,11-dihydro-5,10-methano-5-(3-dimethylaminopropyl)-3-dimethylsulfamoyl-5H-dibenzo[a,d]cycloheptene,
- 23 10,11-dihydro-5,10-methano-5-(3-diethylaminopropyl)-3-dimethylsulfamoyl-5H-dibenzo[a,d]cycloheptene,
- 24 10,11-dihydro-5,10-methano-5-(3-dimethylaminopropyl)-3-trifluoromethyl-5H-dibenzo[a,d]cycloheptene,
- 25 11-acetoxy-10,11-dihydro-5,10-methano-5-(3-methylaminopropyl)-3-trifluoromethyl-5H-dibenzo[a,d]cycloheptene,
- 26 11-benzoyloxy-10,11-dihydro-5,10-methano-5-(3-methylaminopropyl)-5H-dibenzo[a,d]cycloheptene,
- 27 11-chlorobenzoyloxy-10,11-dihydro-5,10-methano-5-(3-dimethylaminopropyl)-5H-dibenzo[a,d]cycloheptene,
- 28 11-p-chlorobenzoyloxy-10,11-dihydro-5,10-methano-5-(3-dimethylaminopropyl)-5H-dibenzo[a,d]cycloheptene,
- 29 11-p-chlorobenzoyloxy-10,11-dihydro-5,10-methano-5-(3-dimethylaminopropyl)-5H-dibenzo[a,d]cycloheptene,
- 30 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-ptosyloxy-5H-dibenzo[a,d]cycloheptene,
- 31 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-ptosyloxy-5H-dibenzo[a,d]cycloheptene,
- 32 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-pmethoxybenzoyloxy-5H-dibenzo[a,d]cycloheptene,
- 33 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-pmethoxybenzoyloxy-5H-dibenzo[a,d]cycloheptene,
- 34 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-ptrifluoromethylbenzoyloxy-5H-dibenzo[a,d]cycloheptene,
- 35 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-ptrifluoromethylbenzoyloxy-5H-dibenzo[a,d]cycloheptene,
- 36 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-ptrifluoromethylbenzoyloxy-5H-dibenzo[a,d]cycloheptene,
- 37 10,11-dihydro-5,10-methano-5-(3-methylaminopropyl)-11-phenoxy-5H-dibenzo[a,d]cycloheptene,
- 38 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-phenoxy-5H-dibenzo[a,d]cycloheptene,
- 39 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-hydrocinnamoyloxy-5H-dibenzo[a,d]cycloheptene,
- 40 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-hydrocinnamoyloxy-5H-dibenzo[a,d]cycloheptene,

- 1 10,11-dihydro-5,10-methano-5-(3-methylaminopropyl)-11-  
2 propionyloxy-5H-dibenzo[a,d]cycloheptene,  
3 11-acetoxyimino-10,11-dihydro-5-(3-dimethylaminopropyl)-3-  
4 dimethylsulfamoyl-5,10-methano-5H-dibenzo[a,d]cycloheptene,  
5 11-benzyloxyimino-10,11-dihydro-5,10-methano-5-(3-methyl-  
6 aminopropyl)-5H-dibenzo[a,d]cycloheptene,  
7 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-  
8 phenylacetoxyimino-5H-dibenzo[a,d]cycloheptene,  
9 11-p-chlorobenzoyloxyimino-10,11-dihydro-5-(3-dimethyl-  
10 aminopropyl)-5,10-methano-5H-dibenzo[a,d]cycloheptene,  
11 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-p-  
12 tosyloxyimino-5H-dibenzo[a,d]cycloheptene,  
13 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-  
14 phenylacetoxyimino-5H-dibenzo[a,d]cycloheptene,  
15 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-  
16 hydrocinnamoyloxyimino-5H-dibenzo[a,d]cycloheptene,  
17 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-  
18 propoxyimino-5H-dibenzo[a,d]cycloheptene,  
19 11-benzenesulfonamido-10,11-dihydro-5-(3-dimethylaminopropyl)-  
20 5,10-methano-5H-dibenzo[a,d]cycloheptene,  
21 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-p-  
22 toluenesulfonamido-5H-dibenzo[a,d]cycloheptene,  
23 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-  
24 phenylmethanesulfonamido-5H-dibenzo[a,d]cycloheptene,  
25 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-5H-  
26 dibenzo[a,d]cycloheptene-N-oxide,  
27 10,11-dihydro-11-dimethylamino-5,10-methano-5-(3-dimethyl-  
28 aminopropyl)-5H-dibenzo[a,d]cycloheptene-N,N'-dioxide,  
29 2-methoxy-10,11-dihydro-5,10-methano-11-hydroxy-5-(3-dimethyl-  
30 aminopropyl)-5H-dibenzo[a,d]cycloheptene,  
31 4-ethoxy-7-trifluoromethyl-10,11-dihydro-5,10-methano-11-hydroxy-  
32 5-(3-dimethylaminopropyl)-5H-dibenzo[a,d]cycloheptene,  
33 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-  
34 hydroxyimino-2-methoxy-5H-dibenzo[a,d]cycloheptene,  
35 10,11-dihydro-5-(3-dimethylaminopropyl)-5,10-methano-11-hydroxy-  
36 imino-4-ethoxy-7-trifluoromethyl-5H-dibenzo[a,d]cycloheptene,  
37 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-dimethylaminopropyl)-  
38 2-methoxy-5H-dibenzo[a,d]cycloheptene,  
39 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-dimethylaminopropyl)-  
40 4-ethoxy-7-trifluoromethyl-5H-dibenzo[a,d]cycloheptene,

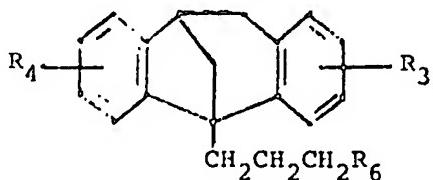
- 1 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-dimethylamino-  
2 propyl)-2-methoxy-5H-dibenzo[a,d]cycloheptene,  
3 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-dimethylamino-  
4 propyl)-4-ethoxy-7-trifluoromethyl-5H-dibenzo[a,d]cyclo-  
5 heptene,  
6 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-diethylaminopropyl)-  
7 2-methoxy-5H-dibenzo[a,d]cycloheptene,  
8 10,11-dihydro-5,10-methano-11-hydroxy-5-(3-diethylaminopropyl)-  
9 4-ethoxy-7-trifluoromethyl-5H-dibenzo[a,d]cycloheptene,  
10 10,11-dihydro-5,10-methano-5-(3-methylaminopropyl)-2-methoxy-  
11 5H-dibenzo[a,d]cycloheptene,  
12 10,11-dihydro-5,10-methano-5-(3-methylaminopropyl)-4-ethoxy-  
13 7-trifluoromethyl-5H-dibenzo[a,d]cycloheptene,  
14 10,11-dihydro-5,10-methano-5-(3-dimethylaminopropyl)-2-methoxy-  
15 5H-dibenzo[a,d]cycloheptene,  
16 10,11-dihydro-5,10-methano-5-(3-dimethylaminopropyl)-4-ethoxy-  
17 7-trifluoromethyl-5H-dibenzo[a,d]cycloheptene,  
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19 5H-dibenzo[a,d]cycloheptene,  
20 10,11-dihydro-5,10-methano-5-(3-diethylaminopropyl)-4-ethoxy-  
21 7-trifluoromethyl-5H-dibenzo[a,d]cycloheptene,  
22 11-acetoxy-10,11-dihydro-5,10-methano-5-(3-methylaminopropyl)-  
23 2-methoxy-5H-dibenzo[a,d]cycloheptene,  
24 11-acetoxy-10,11-dihydro-5,10-methano-5-(3-methylaminopropyl)-  
25 4-ethoxy-7-trifluoromethyl-5H-dibenzo[a,d]cycloheptene,  
26 11-benzoyloxy-10,11-dihydro-5,10-methano-2-methoxy-5-(3-methyl-  
27 aminopropyl)-5H-dibenzo[a,d]cycloheptene,  
28 11-benzoyloxy-10,11-dihydro-5,10-methano-4-ethoxy-7-trifluoro-  
29 methyl-5-(3-methylaminopropyl)-5H-dibenzo[a,d]cycloheptene.

30 The new compounds of my invention possess valuable  
31 pharmacological properties which may be exhibited by tests  
32 on animals. Thus, these new compounds of my invention have an  
33 action on the central nervous system of the intact animal  
34 which reverses the effect of certain depressants. Such com-  
35 pounds are useful in pharmaceutical applications as anti-  
36 depressants.

37 In addition, the new compounds can be used as  
38 starting materials or as intermediate products in the

1 manufacture of other valuable compounds. For example, the  
2 amines form water-insoluble salts with penicillin G and  
3 thus can be utilized in the precipitation and recovery of  
4 penicillin G or other valuable organic acids.

5 The compounds which are especially useful are  
6 compounds which are represented by the general formula:



7 in which:

8 R<sub>3</sub> and R<sub>4</sub> represent an alkyl, an alkoxy, a halo, a trifluoro-  
9 methyl, an alkylsulfonyl or an alkylsulfamoyl sub-  
10 stituent; and in which

11 R<sub>6</sub> represents an amino or an aminoalkyl substituent.

12 In these preferred compounds of my invention, the  
13 R<sub>6</sub> substituent may be a free amino group, but it is preferably  
14 a monoalkylamino, i.e., methylamino, ethylamino, propylamino,  
15 isopropylamino or butylamino, or a dialkylamino substituent  
16 such as diethylamino, dimethylamino, dipropylamino, dibutyl-  
17 amino, or diisopropylamino. In addition, the amino substituent  
18 may form a heterocyclic ring having, together with carbon,  
19 nitrogen or oxygen, from about 5 to 6 atoms in the rings,  
20 including such heterocyclic radicals as N-loweralkyl-  
21 pyrrolidinyl, 1-pyrrolidyl, N-loweralkylpiperidinyl,  
22 N-loweralkylpiperidene-4-morpholinyl and 1-loweralkyl-4-  
23 piperizinyl. Especially effective compounds representative  
24 of the active compounds of my invention are 1-(10,11-dihydro-  
25 5,10-methano-5H-dibenzo[a,d]cycloheptene-5-yl)-3-dimethyl-  
26 amino-1-propanol; 1-(10,11-dihydro-5,10-methano-5H-dibenzo-  
27 [a,d]cycloheptene-5-yl)-3-dimethylamino-1-propanone;

5-(3-dimethylamino-1-propenyl)-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cycloheptene and 5-(3-dimethylaminopropyl)-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cycloheptene.

The processes for preparing the compounds of the present invention are illustrated in the flowsheet wherein X is carboxy or esterified carboxy such as COO-loweralkyl, R<sub>11</sub> is hydroxylcarboxyloxy, R<sub>1</sub> is alkyl or substituted alkyl including aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, or heterocyclicaminoalkyl in which the heterocyclic substituent is attached to the aliphatic side chain through the aminonitrogen atom which is included in a cycle of atoms of carbon, nitrogen or oxygen to form a ring of 5 or 6 atoms, including 1-piperidyl, 1-pyrrolidyl, 4-morpholinyl and 1-loweralkyl-4-piperizinyl and R<sub>3</sub> and R<sub>4</sub> are as defined previously.

In accordance with my invention, a 9-alkanoyl anthracene is heated with an unsaturated lower aliphatic acid such as acrylic acid or an ester thereof (Compound I hereinabove) to form the corresponding 9-alkanoyl-9,10-ethano-11-carboxy or carbalkoxydihydroanthracene (II), and subsequently converting said carboxy or carbalkoxy compound into the corresponding 11-carboxylic acid hydrazide by reaction, for example, of the 11-carboxylic acid ester with hydrazine to form the corresponding 11-carboxylic acid hydrazide, reacting said hydrazide with nitrous acid and hydrolyzing the resulting urethane under acidic conditions to the desired 9-alkanoyl-11-amino-9,10-ethano-9,10-dihydroanthracene (Compound III hereinabove).

The resulting 9-alkanoyl-11-amino-9,10-ethano-9,10-dihydroanthracene is then heated in intimate contact

1 heterocyclicaminoalkyl in which the heterocyclic substituent is  
2 attached to the aliphatic side chain through the aminonitrogen  
3 atom which is included in a cycle of atoms of carbon, nitrogen  
4 or oxygen to form a ring of 5 or 6 atoms, including 1-piperidyl,  
5 1-pyrrolidyl, 4-morpholinyl and 1-loweralkyl-4-piperizinyl,  
6 and in which the dotted line at the 5-position indicates that  
7 the compound may be saturated or unsaturated at the indicated  
8 side chain position ( $C_1$ ,  $C_2$ ).

9           In accordance with my invention, a 9-alkanoyl  
10 anthracene is heated with an unsaturated lower aliphatic  
11 acid such as acrylic acid or an ester thereof (Compound I  
12 hereinabove) to form the corresponding 9-alkanoyl-9,10-  
13 ethano-11-carboxy or carbalkoxydihydroanthracene, and subse-  
14 quently converting said carboxy or carbalkoxy compound into  
15 the corresponding 11-carboxylic acid hydrazide by reaction,  
16 for example, of the 11-carboxylic acid ester with hydrazine  
17 to form the corresponding 11-carboxylic acid hydrazide,  
18 reacting said hydrazide with nitrous acid and hydrolyzing  
19 the resulting urethane under acidic conditions to the  
20 desired 9-alkanoyl-11-amino-9,10-ethano-9,10-dihydroanthra-  
21 cene (Compound III hereinabove).

22           The resulting 9-alkanoyl-11-amino-9,10-ethano-  
23 9,10-dihydroanthracene is then heated in intimate contact  
24 with nitrous acid and an organic acid to form a 5-alkanoyl-  
25 10,11-dihydro-5,10-methano-11-hydroxy or acyloxy-5H-dibenzo-  
26 [a,d]cycloheptone (Compound IV hereinabove).

27           Compound IV is then heated under acidic conditions  
28 in the presence of an amine and an aldehyde, particularly  
29 formaldehyde, to introduce an aminoalkyl, preferably a  
30 dialkylaminomethyl substituent, into the alkanoyl side chain

in a lower alkanol to remove the chloro substituent and produce Compound XIII. Compound XIII is then heated under acidic conditions in the presence of an amine and an aldehyde to introduce an aminoalkyl substituent into the alkanoyl side chain and form the desired compound XIV which is reduced to Compound VIII by heating in the presence of an alkali metal borohydride.

The formed aminoalkanol VIII is then dehydrated by heating in the presence of an acidic dehydrating agent such as phosphorus oxychloride, whereby a double bond is introduced into the 5-position side chain of the compound and there is formed a 5-alkylaminoalkenyl-5,10-methano-10,11-dihydro-5H-dibenzo [a,d]cycloheptene IX. This compound IX is then catalytically hydrogenated to saturate the side chain double bond with resultant formation of a 5-alkyl-aminoalkyl-5,10-methano-10,11-dihydro-5H-dibenzo [a,d]cycloheptene X.

Thus, the process of my invention involves the conversion of a 9-akanoylanthracene compound to produce a 5,10-methano-10,11-dihydro-5H-dibenzo [a,d]cycloheptene containing an alkylaminoalkyl substituent attached to the 5-position.

It is, of course, clear that many variations of the above-mentioned process may be employed but, as such, they are presumed to be included within the scope of my invention. Thus, my process involves the addition

1 of an unsaturated compound across the 9,10-position of  
2 the 9-alkanoylanthracene starting material, rearrangement  
3 of the resulting 9,10-ethano-9,10-dihydroanthracene under  
4 acidic conditions to produce the desired 5,10-methano-  
5 10,11-dihydro-5H-dibenzo[a,d]cycloheptene nucleus, and  
6 elaboration of the alkanoyl side chain at the 5-position  
7 of said 5,10-methano compound to produce a 5,10-methano-  
8 10,11-dihydro-5H-dibenzo[a,d]cycloheptene having an alkyl-  
9 aminoalkyl side chain at the 5-position. The details of  
10 this process are set forth hereinbelow.

11 In converting 9-alkanoylanthracene, e.g., 9-acetyl-  
12 9-propionoyl-9-butyryl-9-valeryl or 9-hexanoylanthracene to  
13 the corresponding 9-alkanoyl-9,10-ethano-11-carboxy or carb-  
14 alkoxy dihydroanthracene, the starting material is heated  
15 with acrylic acid or a derivative thereof as, for example,  
16 a loweralkyl ester, to produce the corresponding 9-alkanoyl-  
17 11-carboxy or carbalkoxy-9,10-ethanodihydroanthracene. In  
18 carrying out the reaction, it is preferable to heat a mixture  
19 of the reactants at the reflux temperature for a period of  
20 from a few minutes to 24 hours and, preferably, for a period  
21 of about 1 to 3 hours.

22 The reaction may be conducted in the presence of  
23 an inert high boiling solvent either as a liquid aromatic  
24 compound including phenol ethers, halogenated or nitro-  
25 substituted benzene, such as anisole, o-dichlorobenzene,  
26 nitrobenzene, and the like. However, it is preferred in  
27 the present instance to carry out the reaction by heating a  
28 mixture of the alkanoylanthracene and the acrylic acid or  
29 derivative thereof together for the recommended period of  
30 time using excess acrylic acid derivative as solvent medium.

1 Acrylic acid derivatives which may be used as reactants in  
2 this addition reaction include methyl, ethyl, propyl, iso-  
3 propyl, butyl, amyl and hexyl esters of acrylic acid. The  
4 product obtained in the case of the 11-carboxylic acid  
5 derivative is readily separated from the reaction mixture  
6 by dissolving in aqueous alkali and precipitation from acid,  
7 followed by recrystallization from mixtures of lower alkanols  
8 and water.

9 In carrying out the reaction with lower alkyl  
10 ester of acrylic acid, it is preferred to conduct the reaction  
11 in a dry, inert solvent in the presence of a small amount of  
12 an acidic catalyst such as the halide of aluminum, and heat  
13 the entire reaction mixture for a period of from about 2 to  
14 50 hours and, preferably, for a period of from about 15 to  
15 30 hours. Following reaction, the entire mixture is diluted  
16 with an aqueous acid and the solvent layer containing the  
17 formed product is separated, washed and dried. The product  
18 is obtained by crystallization from a concentrated solution.

19 The formed 9-alkanoyl-11-carboxy or carbalkoxy  
20 9,10-ethanodihydroanthracene (Compound II hereinabove) is  
21 then converted to the corresponding 9-alkanoyl-11-amino-  
22 9,10-ethano-9,10-dihydroanthracene by, first, conversion  
23 to the acid azide and degradation to the amino compound.  
24 This is conveniently accomplished either by reaction of  
25 the free acid with hydrazoic acid, whereby the 11-amino  
26 compound is formed directly or by first converting the  
27 loweralkyl ester by reaction with hydrazine to the corres-  
28 ponding hydrazide. Reaction of the thus-formed hydrazide  
29 with nitrous acid results in production of the intermediate  
30 11-urethane which is readily hydrolyzed under acidic

1 conditions to the corresponding 11-amino-9,10-dethanodi-  
2 hydroanthracene.

3 In carrying out the conversion of the 11-carboxy  
4 or 11-carbalkoxy-9-alkanoyl-9,10-dihydroanthracene to the  
5 corresponding 11-amino compound, it is preferred to first  
6 protect the 9-alkanoyl side chain as, for example, by  
7 formation of a ketal of the side chain substituent. This  
8 may be conveniently done by reaction of the 9-alkanoyl-11-  
9 carboxy or carbalkoxy-9,10-ethanoanthracene with a lower-  
10 alkanol or a 1,2 or 1,3 loweralkylene glycol, such as  
11 ethylene glycol, 1,3-propylene glycol, or butane-diol  
12 (1,2 or 1,3) in the presence of an acid.

13 In the preferred instance, the 11-carboxy-9-  
14 alkanoyl-9,10-ethanodihydroanthracene or the corresponding  
15 ester thereof is heated in the presence of ethylene glycol  
16 admixed with a catalytic amount of an acid such as p-toluene-  
17 sulfonic acid, to form the corresponding dioxolane of the  
18 side chain carbonyl substituent.

19 Conversion of the thus-formed alkyl-9,10-dihydro-  
20 9-(1-alkylenedioxyalkyl)-9,10-ethano-11-carboxy compound to  
21 the corresponding 11-carboxy ester is carried out in the  
22 same manner as previously described for the corresponding  
23 9-alkanoyl-9,10-ethano-11-carboxy-9,10-dihydroanthracene  
24 compounds. The resulting esterified dioxolane derivative  
25 is then reacted with hydrazine to form the corresponding  
26 carboxylic acid hydrazide. The formed hydrazide is then  
27 heated with nitrous acid to form the 11-amino derivative.  
28 When the dioxolane derivative is used, rearrangement of the

1 11-carboxylic acid hydrazide to the 11-amino compound  
2 results in simultaneous hydrolysis of the dioxolane moiety,  
3 and regeneration of the 9-alkanoyl side chain.

4 The resulting 9-alkanoyl-11-amino-9,10-ethano-  
5 dihydroanthracene is then heated with nitrous acid to form  
6 5-alkanoyl-5,10-methano-11-hydroxy-5H-dibenzo [a,d]cyclo-  
7 heptene (Compound IV hereinabove).

8 When the reaction is carried out in a solvent  
9 which is unreactive with the formed product, the compound  
10 is readily isolated by evaporation of the solvent and  
11 separation of the product in crude form. In the event that  
12 the reaction is carried out in a loweralkanoic acid, the  
13 product obtained is the 11-acyloxy compound corresponding  
14 thereto wherein the 11-hydroxyl substituent is esterified by  
15 reaction with the reacting solvent alkanoic acid. In a  
16 preferred instance of the reaction, a 9-alkanoyl-11-amino-  
17 9,10-ethano-9,10-dihydroanthracene is heated in contact with  
18 nitrous acid in a solution of glacial acetic acid to form  
19 a mixture of products comprising principally the 11-acetoxy  
20 derivative of 5-alkanoyl-5,10-methano-5H-dibenzo [a,d]cyclo-  
21 heptene, along with a small amount of the corresponding  
22 11-hydroxy derivative.

23 The resulting product, i.e., the 11-acyloxy or  
24 the 11-hydroxy compound (Compound IV hereinabove) is then  
25 heated under acidic conditions in the presence of an amine  
26 and an aldehyde in order to elaborate the side chain alkanoyl  
27 substituent and form a 5-dialkylaminoalkanoyl-5,10-methano-  
28 10,11-dihydro-5H-dibenzo [a,d]cycloheptene. This reaction is  
29 preferably carried out by reaction of formaldehyde and a  
30 secondary amine such as a dialkylamine or a heterocyclic

1 amine wherein the amino nitrogen is included in the 5 or 6-  
2 membered heterocyclic ring comprising carbon, nitrogen and/or  
3 oxygen and sulfur, preferably a diloweralkylamine, with  
4 Compound IV hereinabove either present as the 11-acyloxy,  
5 the 11-hydroxy, or the corresponding compound containing  
6 only hydrogen as a substituent at the 11-position. The  
7 compound which is formed (indicated as Compound V herein-  
8 above) is the corresponding 5-dialkylaminoalkanoyl-5,10-meth-  
9 ano-5H-dibenzo[a,d]cycloheptene having an acyloxy, a hydroxy,  
10 or hydrogen substituent at the 11-position.

11           The reaction is preferably carried out by mixing  
12 the dialkylamine as the acid salt as, for example, a hydro-  
13 chloride, with paraformaldehyde and an inert organic solvent,  
14 hydrocarbon solvents being preferred such as benzene, nitro-  
15 benzene, and the like. The entire reaction mixture is heated  
16 to from 50°C. to the reflux temperature of the reaction  
17 mixture for a period of from a few minutes to 24 hours,  
18 preferably for a period of time of about 15 minutes to 1  
19 hour. Higher temperatures may be employed but they are  
20 impractical since the reaction goes essentially to completion  
21 in a short time at the reflux temperature of the mixture.

22           Following the reaction, during which the desired  
23 dialkylaminoalkanoyl-5,10-methanodibenzocycloheptene is  
24 formed, the water formed during the reaction is distilled as  
25 an azeotrope and the product precipitates as the acid salt  
26 which may be recovered by filtration. The resulting alkyl-  
27 aminoalkanoyl compound is then reduced by reaction with an  
28 alkali metal borohydride such as potassium or sodium boro-  
29 hydride, to the corresponding dialkylaminoalkanol-  
30 substituted compound (Compound VI hereinabove).

1           In the event the dialkylaminoalkanoyl compound  
2 submitted to this reduction procedure contains an acyloxy  
3 substituent at the 11-position in accordance with one of  
4 the preferred embodiments of my invention the acyloxy sub-  
5 stituent is hydrolyzed during the course of the reduction  
6 reaction and the formed product is recovered as the  
7 11-hydroxy derivative thereof. Thus, reaction of the corres-  
8 ponding 1-(10,11-dihydro-5,10-methano-11-acetoxy-5H-dibenzo-  
9 [a,d]cyclohepten-5-yl)-3-dimethylamino-1-propanone results  
10 in formation of 1-(10,11-dihydro-5,10-methano-11-hydroxy-  
11 5H-dibenzo [a,d]cyclohepten-5-yl)-3-dimethylamino-1-propanol.

12           Similarly, reaction of 1-(10,11-dihydro-5,10-  
13 methano-5H-dibenzo [a,d]cyclohepten-5-yl)-3-dimethylamino-  
14 1-propanone with potassium borohydride results in the pro-  
15 duction of the corresponding 3-dimethylamino-1-propanol  
16 compound.

17           The reaction may be carried out from 0°C. to  
18 100°C., although it is preferably carried out at from 15 to  
10 30°C. under aqueous conditions. The starting 1-propanone  
20 compound, being only partly soluble in water, is dissolved  
21 in a loweralkanol as, for example, methanol, ethanol,  
22 propanol, and the like, and is mixed with a solution of the  
23 alkali metal borohydride, e.g., sodium or potassium boro-  
24 hydride in water made slightly alkaline with sodium hydroxide.

25           The product of the reduction reaction is convenient-  
26 ly recovered as the acid salt thereof by removal of the solvent  
27 by distillation under reduced pressure and extraction of the  
28 residual reaction mixture with benzene. The acid salt as,  
29 for example, the fumarate, is then purified by recrystalliza-  
30 tion from a solution of a loweralkanol, e.g., ethanol. The

1 product obtained in this manner may then be dehydrated  
2 by heating in the presence of an acidic dehydrating agent  
3 as, for example, phosphorus oxychloride and phosphorus  
4 pentoxide, and the like. The aminoalkanol (Compound VI  
5 hereinabove) in solution in benzene or chloroform or other  
6 inert solvents, is mixed with an excess amount of phosphorus  
7 oxychloride and heated to the reflux temperature of the  
8 solvent for a period of from 1 to 30 hours at reflux  
9 temperature.

10           The product obtained as a result of the dehydra-  
11 tion reaction is the desired 5-dialkylaminoalkenyl-5,10-  
12 methano-5H-dibenzo[a,d]cycloheptene (Compound VII herein-  
13 above) mixed with the corresponding 5(1-chloro-3-dialkylamino)  
14 compound wherein the dotted line of the formula represents  
15 a double bond in the indicated position of the side chain.  
16 The unsaturated product and (or the halo-substituted product)  
17 obtained in this manner is then catalytically reduced to  
18 saturate the side chain and produce the corresponding 5-  
19 alkylaminoalkyl-5,10-methano-10,11-dihydro-5H-dibenzo[a,d]  
20 cycloheptene.

21           The compounds of my invention can advantageously  
22 be employed in pharmaceutical applications because they  
23 have been found to possess antidepressant activity. As  
24 antidepressants, they may be administered orally in the form  
25 of tablets, powders, sustained release pellets and the like  
26 or they may be administered orally or parenterally in the  
27 form of aqueous solutions or suspensions. When administered  
28 orally or parenterally, satisfactory results are obtained  
29 at a daily dosage level of from about 1 mg. to about 300 mgs.  
30 preferably given in divided doses over the day or in sus-  
31 tained release form. The compounds are preferably

1 administered in the form of their non-toxic acid addition  
2 salts and these salts are included within the scope of this  
3 invention. In addition, the 5,10-methanodibenzocycloheptene  
4 compounds represented by Formulas VI and VII may be converted  
5 to the N oxides. These compounds, as well as their acid  
6 addition salts, possess antidepressant activity and are  
7 also included within the scope of my invention.

8 The following examples are presented to illustrate  
9 the methods of carrying out the present invention.

10                   Example 1

11                   9-Acetyl-9,10-dihydro-9,10-ethanoanthracene-11-carboxylic  
12                   acid

13                   A solution of 9-acetylanthracene (11.6 g., 0.0525  
14 mole) in 30 ml. of acrylic acid (stabilized with p-methoxy-  
15 phenol) is heated to refluxing for 2-1/2 hours. The cooled,  
16 viscous mixture is dissolved in 20% aqueous sodium hydroxide  
17 while cooling in an ice bath. The resulting solution is  
18 added to an excess of ice-cold 6 N. hydrochloric acid and  
19 the gummy precipitate collected, washed with water, and  
20 crystallized from a mixture of ethanol and water with  
21 decolorization with decolorizing carbon. The white crystal-  
22 line 9-acetyl-9,10-dihydro-9,10-ethanoanthracene-11-carboxy-  
23 lic acid, m.p. 169-171°C dec., when recrystallized from  
24 ethanol-water, gives product, m.p. 172-174°C. dec. A  
25 purified sample melts at 172.5-174.5°C. dec.

26                   Anal. calc'd. for C<sub>19</sub>H<sub>16</sub>O<sub>3</sub>: C, 78.06; H, 5.52.

27                   Found: C, 77.94; H, 5.50.

28                   Example 2

29                   9,10-Dihydro-9-(2-methyl-1,3-dioxolan-2-yl)-9,10-ethano-  
30                   anthracene-11-carboxylic acid

31                   9-Acetyl-9,10-dihydro-9,10-ethanoanthracene-11-

1 carboxylic acid (2.5 g., 0.00855 mole), p-toluene sulfonic  
2 acid monohydrate (100 mg.), ethylene glycol (8 ml.) and  
3 dry toluene (75 ml.) are mixed and heated to refluxing  
4 under a Dean-Stark water separator for 12 hours. Solvent  
5 is evaporated under reduced pressure. The residual oil  
6 containing the product is dissolved in 10 ml. of 95%  
7 ethanol and heated to refluxing with 10 ml. of 10% aqueous  
8 sodium hydroxide for 1-1/2 hours. Ethanol is distilled  
9 under reduced pressure and the residual alkaline solution  
10 diluted with water and added to an excess of ice-cold 6 N  
11 hydrochloric acid. The precipitate is collected, washed  
12 with water, and crystallized from 50% ethanol, m.p. 239-246°C.  
13 A purified sample melts at 250-252°C. after repeated re-  
14 crystallizations from 50% alcohol.

15 Anal. calc'd. for  $C_{21}H_{20}O_4$ : C, 74.99; H, 5.99.  
16 Found: C, 74.62; H, 5.99.

17 Example 3

18 Methyl-9,10-dihydro-9-(2-methyl-1,3-dioxolan-2-yl)-9,10-  
19 ethanoanthracene-11-carboxylate

20 A dry ethereal solution (50 ml.) containing  
21 about 1.4 g. (0.033 mole) of diazomethane is added to a  
22 stirred suspension of 9,10-dihydro-9-(2-methyl-1,3-  
23 dioxolan-2-yl)-9,10-ethanoanthracene-11-carboxylic acid  
24 (1.95 g., 0.0058 mole) in 50 ml. of absolute ether cooled  
25 in an ice bath. The ice bath then is removed and the  
26 mixture stirred at room temperature overnight. Solvent is  
27 evaporated at room temperature and under reduced pressure  
28 and the residue dissolved in absolute ether. After  
29 filtration from a small amount of insoluble material, the

1 solution is evaporated and the residual colorless glass  
2 containing the product crystallized from a mixture of  
3 ethanol and water, m.p. 128-131°C. Repeated recrystall-  
4 lizations from 60% ethanol give a purified product,  
5 m.p. 128-130°C.

6 Anal. calc'd for  $C_{22}H_{22}O_4$ : C, 75.41; H, 6.33.  
7 Found: C, 75.39, H, 6.23.

8                   Example 4

9                   Methyl-9-acetyl-9,10-dihydro-9,10-ethanoanthracene-11-  
10                   carboxylate

11                  A solution of 9-acetyl-9,10-dihydro-9,10-  
12 ethanoanthracene-11-carboxylic acid (2.92 g., 0.01 mole)  
13 and p-toluenesulfonic acid monohydrate (100 mg.) in 60 ml.  
14 of absolute methanol is heated to refluxing for 3-1/2 hours.  
15 Solvent is evaporated under reduced pressure and the residual  
16 oil dissolved in benzene (30 ml.). After washing with 5%  
17 aqueous sodium hydroxide and water and drying by filtration  
18 through anhydrous magnesium sulfate, the benzene is evapo-  
19 rated under reduced pressure. The residue consists of the  
20 crystalline product, m.p. 90-94°C. A purified sample melts  
21 at 95-97°C., after repeated recrystallizations from ether-  
22 petroleum ether.

23                  Anal. calc'd. for  $C_{20}H_{18}O_3$ : C, 78.41; H, 5.92.  
24                  Found: C, 78.93; H, 5.81.

25                   Example 5

26                   Methyl-9-acetyl-9,10-dihydro-9,10-ethanoanthracene-11-  
27                   carboxylate

28                  A solution of methyl acrylate (34.4 g., 0.4 mole,  
29 freshly redistilled under nitrogen, b.p. 78.5 - 79.5°C.) in  
30 40 ml. of dry benzene is added dropwise over a 10 minute  
31 period to a stirred suspension of anhydrous aluminum

1 chloride (5.33 g., 0.04 mole) in 180 ml. of dry benzene  
2 warmed to about 50°C. The clear solution is stirred and  
3 maintained at about 50°C. while a solution of 9-acetyl-  
4 anthracene (44. g., 0.2 mole) in 50 ml. of dry benzene is  
5 added. The mixture is stirred and heated in a slow stream  
6 of nitrogen at 60-65°C. for 21 hours. After cooling the  
7 mixture in an ice-bath, 100 ml. of 6 N. hydrochloric acid  
8 is added. The benzene layer is separated, re-extracted  
9 with 100 ml. 6 N. hydrochloric acid, washed with three  
10 100 ml. portions of water, and dried over anhydrous sodium  
11 sulfate. Evaporation of the benzene under reduced pressure  
12 and crystallization of the oily residue from a mixture of  
13 hexane and benzene affords the product, m.p. 101-103°C.  
14 This product gives no depression in melting point on ad-  
15 mixture with an authentic sample of methyl-9-acetyl-9,10-  
16 dihydro-9,10-ethanoanthracene-11-carboxylate prepared by  
17 the procedure described in Example 4.

18                   Example 6

19 Methyl-9,10-dihydro-9-(2-methyl-1,3-dioxolan-2-yl)-9,10-  
20 ethanoanthracene-11-carboxylate

21                   Methyl-9-acetyl-9,10-dihydro-9,10-ethanoanthra-  
22 cene-11-carboxylate (46 g., 0.15 mole), p-toluenesulfonic  
23 acid monohydrate (500 mg.), ethylene glycol (46 ml.) and  
24 dry benzene (550 ml.) are mixed and heated to refluxing  
25 under a Dean-Stark water separator for 8 hours. The mixture  
26 is transferred to a separatory funnel, the lower ethylene  
27 glycol phase removed, and the benzene phase washed with  
28 several 50 ml. portions of water. After drying by filtration  
29 through anhydrous sodium sulfate, the benzene is evaporated  
30 under reduced pressure and the residual oil comprising the

1 product crystallized from 30 ml. of 95% ethanol, m.p.

2 127-130°. Recrystallization from 95% ethanol gives product  
3 with m.p. 128.5-130.5°.

4

Example 7

5 9,10-Dihydro-9-(2-methyl-1,3-dioxolan-2-yl)-9,10-ethano-  
6 anthracene-11-carboxylic acid hydrazide

7 Methyl-9-acetyl-9,10-dihydro-9-(2-methyl-1,3-  
8 dioxolan-2-yl)-9,10-ethanoanthracene-11-carboxylate (1.5 g.,  
9 0.0043 mole) is suspended in 7 ml. of hydrazine hydrate  
10 and the mixture is heated to refluxing for 15 minutes.

11 Sufficient ethanol (5 ml.) is added to dissolve the suspended  
12 oil and the solution is heated to refluxing for 3 hours.

13 During this period, white crystals separate and after cooling,  
14 the precipitate is collected and washed with 50% ethanol,  
15 m.p. 253-254°C. Repeated recrystallizations from absolute  
16 ethanol give an analytical sample, m.p. 254-255°C.

17 Anal. calc'd. for  $C_{21}H_{22}N_2O_3$ : C, 72.26; H, 6.06,  
18 N, 8.03. Found: C, 71.97; H, 6.27, N, 8.04.

19

Example 8

20 9,10-Dihydro-11-ethoxy carbonylamino-9-(2-methyl-1,3-dioxolan-2-yl)-9,10-ethanoanthracene

22 A suspension of 9,10-dihydro-9-(2-methyl-1,3-  
23 dioxolan-2-yl)-9,10-ethanoanthracene-11-carboxylic acid  
24 hydrazide (4.8 g., 0.0133 mole) in 190 ml. of acetone is  
25 stirred and cooled to 0°C. in an ice-salt bath. The solid is  
26 dissolved by the addition of 9 ml. of 6 N. hydrochloric acid.  
27 A solution of sodium nitrite (965 mg., 0.014 mole) in 6 ml.  
28 of water is added dropwise and stirring at -5° to 0°C. is  
29 continued for 30 minutes. After the addition of 190 ml. of  
30 absolute ethanol and a 15 minute period of stirring at 0°C.  
31 the mixture is filtered. The filtrate is stirred with

7 oxychloride and heated to the reflux temperature of the  
8 solvent for a period of from 1 to 30 hours at reflux  
9 temperature.

10           The product obtained as a result of the dehydra-  
11 tion reaction is the desired 5-dialkylaminoalkenyl-5,10-  
12 methano-5H-dibenzo[a,d]cycloheptene (Compound VII herein-  
13 above) mixed with the corresponding 5(1-chloro-3-dialkylamino)  
14 compound wherein the dotted line of the formula represents  
15 a double bond in the indicated position of the side chain.  
16 The unsaturated product and (or the halo-substituted product)  
17 obtained in this manner is then catalytically reduced to  
18 saturate the side chain and produce the corresponding 5-  
19 alkylaminoalkyl-5,10-methano-10,11-dihydro-5H-dibenzo[a,d]  
20 cycloheptene.

21           The compounds of my invention can advantageously  
22 be employed in pharmaceutical applications because they  
23 have been found to possess antidepressant activity. As  
24 antidepressants, they may be administered orally in the form  
25 of tablets, powders, sustained release pellets and the like  
26 or they may be administered orally or parenterally in the  
27 form of aqueous solutions or suspensions. When administered  
28 orally or parenterally, satisfactory results are obtained  
29 at a daily dosage level of from about 1 mg. to about 300 mgs.  
30 preferably given in divided doses over the day or in sus-  
31 tained release form. The compounds are preferably

1                   Example 10

2    11-Acetoxy-5-acetyl-10,11-dihydro-5,10-methano-5H-dibenzo-  
3    [a,d]cycloheptene and 5-acetyl-10,11-dihydro-5,10-methano-  
4    5H-dibenzo[a,d]cyclohepten-11-ol  
5                   9-Acetyl-11-amino-9,10-dihydro-9,10-ethano-  
6    anthracene hydrochloride (4.2 g.; 0.014 mole) is suspended  
7    in 40 ml. of glacial acetic acid and stirred while sodium  
8    nitrite (3.9 g., 0.056 mole) is added in portions over  
9    10-15 minutes. The temperature rises spontaneously to about  
10   42°C. and gas evolution is vigorous. After stirring for  
11   22 hours at room temperature, the reaction mixture containing  
12   the product is filtered, washing the precipitate with glacial  
13   acetic acid. Distillation of the acetic acid from the filtrate  
14   under reduced pressure leaves a viscous oil containing a  
15   mixture of 11-acetoxy-5-acetyl-10,11-dihydro-5,10-methano-  
16   5H-dibenzo[a,d]cycloheptene and 5-acetyl-10,11-dihydro-5,10-  
17   methano-5H-dibenzo[a,d]cyclohepten-11-ol that solidifies on  
18   trituration with cold methanol. The precipitate is collected  
19   and recrystallized from methanol, m.p. 141-144°C. Repeated  
20   recrystallization of the product from methanol gives 11-ace-  
21   toxy-5-acetyl-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]-  
22   cycloheptene melting at 142-144°C.

23                   Anal. calc'd. for  $C_{20}H_{18}O_3$ : C, 78.41; H, 5.92.

24   Found: C, 78.48; H, 6.00.

25                   The methanol filtrate from the precipitation of  
26    11-acetoxy-5-acetyl-10,11-dihydro-5,10-methano-5H-dibenzo-  
27    [a,d]cycloheptene is evaporated. The residual oily solid  
28   is freed from oil by pressing out on a porous plate yielding 5-  
29   acetyl-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cyclohepten-11-  
30   ol), m.p. 136-163°C. A typical sample melts at 178.5-179.5°C.

1 after successive recrystallizations from ethanol-water,  
2 isopropyl alcohol-water and absolute ether.

3 Anal. calc'd. for  $C_{18}H_{16}O_2$ : C, 81.79; H, 6.10.  
4 Found: C, 81.82; H, 6.09.

5                   Example 11

6 5-Acetyl-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cyclo-  
7 hepten-11-ol

8                   11-Acetoxy-5-acetyl-10,11-dihydro-5,10-methano-  
9 5H-dibenzo[a,d]cycloheptene (1.8 g.) is dissolved in 30 ml.  
10 of 5% potassium hydroxide in 95% ethanol and the solution  
11 is heated to refluxing for 1-1/2 hours. Evaporation of the  
12 ethanol under reduced pressure and trituration of the residue  
13 with water gives the solid product which is collected, dried,  
14 and recrystallized from ether to obtain substantially pure  
15 product, m.p. 167-177°. Recrystallization from ether  
16 gives product, m.p. 174-177°.

17                   Example 12

18 1-(11-Acetoxy-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]-  
19 cyclohepten-5-yl)-3-dimethylamino-1-propanone hydrochloride

20                   A mixture of dimethylamine hydrochloride (165 mg.,  
21 0.00202 mole), paraformaldehyde (70 mg., 0.00233 mole) and  
22 concentrated hydrochloric acid (1 drop) is stirred and heated  
23 to refluxing in 1 ml. of nitrobenzene and 1 ml. of benzene  
24 for 20 minutes. During this period, the solids first form  
25 a ball and then a colorless, lower second phase. 11-Acetoxy-  
26 5-acetyl-5,10-methano-5H-dibenzo[a,d]cycloheptene (610 mg.,  
27 0.002 mole) is added and the mixture is stirred at reflux  
28 for 2 hours. During the last 5 minutes of this period, the  
29 condenser is removed so that water in the mixture may distill  
30 azeotropically. After cooling to room temperature and

1 filtration from a small quantity of precipitate, the filtrate  
2 is diluted with ether. The product precipitates and is  
3 collected, washed with ether, dried, and crystallized from  
4 isopropyl alcohol-ether, m.p. 181-183°C. dec. Repeated  
5 recrystallizations from isopropyl alcohol-ether give a  
6 purified product, m.p. 186-187°C. dec.

7 Anal. calc'd for  $C_{23}H_{25}NO_3 \cdot HCl$ : C, 69.07; H, 6.55;  
8 N, 3.50. Found: C, 68.85; H, 6.71; N, 3.37.

9                   Example 13

10 1-(10,11-Dihydro-11-hydroxy-5,10-methano-5H-dibenzo[a,d]..  
11 cyclohepten-5-yl)-3-dimethylamino-1-propanol

12                 1-(11-Acetoxy-10,11-dihydro-5,10-methano-5H-  
13 dibenzo[a,d]cyclohepten-5-yl)-3-dimethylamino-1-propanone is  
14 prepared from 4.22 g. (0.0105 mole) of the hydrochloride salt  
15 by rendering an aqueous solution of the salt strongly alkaline  
16 with 5% sodium hydroxide and extracting the oily base into  
17 benzene. Evaporation of the washed and dried benzene extract  
18 under reduced pressure leaves the oily residue which is  
19 dissolved in 250 ml. of methanol. A solution of potassium  
20 borohydride (1.13 g., 0.021 mole) in 6 ml. of water containing  
21 2 drops of 10 N. sodium hydroxide is added. After stirring  
22 for 6 hours and standing for 2 days at room temperature,  
23 methanol is distilled under reduced pressure. The residue is  
24 partitioned between benzene and water and the benzene extract  
25 is separated, washed, dried, and evaporated to dryness under  
26 reduced pressure. The product remains as the residual glass  
27 in quantitative yield. The base is converted to the hydrogen  
28 oxalate salt by treating an ethanolic solution with an  
29 equimolar amount of oxalic acid dissolved in ethanol. The  
30 1-(10,11-dihydro-11-hydroxy-5,10-methano-5H-dibenzo[a,d] -

1 cyclohepten-5-yl)-3-dimethylamino-1-propanol hydrogen oxalate  
2 precipitates, m.p. 195-197°C. A purified sample melts at  
3 199-200°C. after repeated recrystallizations from mixtures  
4 of absolute ethanol and methanol.

5 Anal. calc'd for  $C_{21}H_{25}NO_2 \cdot C_2H_2O_4$ : C, 66.81,  
6 H, 6.58, N, 3.39. Found: C, 66.55; H, 6.52; N, 3.51.

7 Example 14

8 1-(11-Chloro-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cyclo-  
9 hepten-5-yl)-3-dimethylamino-1-propanol hydrochloride

10 1-(10,11-Dihydro-11-hydroxy-5,10-methano-5H-  
11 dibenzo[a,d]cyclohepten-5-yl)-3-dimethylamino-1-propanol  
12 (0.75 g.; 0.00232 mole) is added in portions to 2.5 ml. of  
13 thionyl chloride with stirring and cooling in an ice bath.  
14 After 3-1/2 hours of stirring at room temperature, the excess  
15 thionyl chloride is distilled under reduced pressure and at  
16 room temperature. The residual glass is dissolved in absolute  
17 ethanol and the solution evaporated under reduced pressure.  
18 Addition and removal of ethanol is repeated and, finally,  
19 the residue is triturated with 3 ml. of acetone. The white  
20 crystalline hydrochloride of the product is collected, washed  
21 with ether and dried in vacuo, m.p. 182-190°C. dec. A  
22 purified sample melts at 192-194°C. dec. after recrystalli-  
23 zation from acetone.

24 Anal. calc'd for  $C_{21}H_{24}ClNO \cdot HCl$ : C, 66.68, H, 6.66,  
25 Cl, 18.74. Found: C, 66.64; H, 6.65; Cl, 18.66.

26 Example 15

27 1-(10,11-Dihydro-5,10-methano-5H-dibenzo[a,d]cyclohepten-5-yl)-  
28 3-dimethylamino-1-propanol

29 A dry, nitrogen-flushed flask is charged with  
30 1-(11-chloro-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]-

1 mixture evaporated under reduced pressure. Crystallization  
2 of the residue from 95% ethanol affords the product, m.p.  
3 126-130°C. A purified sample melts at 128.5-130.5°C  
4 after repeated recrystallizations from 95% ethanol.

5 Anal. calc'd. for  $C_{18}H_{15}ClO$ : C, 76.45; H, 5.35;  
6 Cl, 12.54. Found: C, 76.23; H, 5.44; Cl, 12.52.

7               Example 18

8       5-Acetyl-10,11-dihydro-5,10-methano-5H-dibenzo [a,d] cyclo-  
9       heptene

10              A solution of 5-acetyl-11-chloro-10,11-dihydro-  
11 5,10-methano-5H-dibenzo [ad] cycloheptene (0.84 g., 0.00308  
12 mole) in 0.5 ml. triethylamine - 35 ml. absolute ethanol  
13 is hydrogenated at room temperature and atmospheric pressure  
14 in the presence of 70 mg. of 5% palladium on charcoal. When  
15 one equivalent of hydrogen is taken up, the reduction stops  
16 and catalyst is removed by filtration and washed with  
17 absolute ethanol. The filtrate is evaporated under reduced  
18 pressure and the residue triturated with absolute ether. The  
19 precipitate of triethylamine hydrochloride is removed by  
20 filtration, the filtrate evaporated and the residual solid  
21 crystallized from 95% ethanol, m.p. 105-107°C. A purified  
22 sample melts at 106-107°C. after recrystallization from 70%  
23 ethanol and sublimation at 80° and 0.05 mm.

24              Anal. calc'd. for  $C_{18}H_{16}O$ : C, 87.06; H, 6.50.  
25 Found: C, 87.00; H, 6.38.

26               Example 19

27       1-(10,11-Dihydro-5,10-methano-5H-dibenzo [a,d] cyclohepten-5-yl)-  
28       3-dimethylamino-1-propanone

29              A mixture of dimethylamine hydrochloride (265 mg.,  
30 0.00324 mole) paraformaldehyde (112 mg., 0.00372 mole) and

1 cyclohepten-5-yl)-3-dimethylamino-1-propanol hydrochloride  
2 (0.855 g., 0.00225 mole), tert-butyl alcohol (3.35 g.,  
3 0.045 mole) and 20 ml. of dry tetrahydrofuran. Under a slow  
4 stream of nitrogen, the suspension is stirred vigorously  
5 and freshly-cut small pieces of sodium (1.35 g.; 0.0575 g.  
6 atom) are added. The mixture is stirred and heated to reflux-  
7 ing for 6 hours. Excess sodium is destroyed by the slow  
8 addition of 10 ml. of absolute methanol. After cooling,  
9 the mixture is poured into 250 ml. of ice water and the  
10 oily base is extracted into 1:1 benzene-ether. Solvents are  
11 distilled from the washed and dried organic extract under  
12 reduced pressure, leaving the oily product as the residue.

13 The base (0.6 g., 0.00196 mole) is converted to  
14 the fumarate salt by treating an ethanolic solution with an  
15 equimolar amount of fumaric acid dissolved in ethanol. The  
16 1-(10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cyclohepten-  
17 5-yl)-3-dimethylamino-1-propanol fumarate precipitates, m.p.  
18 231-233°C. dec. An analytical sample melts at 232-233°C.  
19 dec. after recrystallization from absolute ethanol.

20 Anal. calc'd. for  $C_{23}H_{27}NO_3 \cdot 1/2C_4H_4O_4$ : C, 75.59;  
21 H, 7.45; N, 3.83. Found: C, 75.28; H, 7.38; N, 3.76.

22 Example 16

23 1-(10,11-Dihydro-5,10-methano-5H-dibenzo[a,d]cyclohepten-5-yl)-  
24 3-dimethylamino-1-propanol

25 With a stream of nitrogen passing through the  
26 solution, 55% hydriodic acid, 0.2 ml., is heated on the  
27 steam bath and decolorized by the addition of 1 drop of 50%  
28 hypophosphorous acid. Red phosphorus (25 mg., 0.0008 g.  
29 atom), 1-(10,11-dihydro-11-hydroxy-5,10-methano-5H-dibenzo-  
30 [a,d]cyclohepten-5-yl)-3-dimethylamino-1-propanol (66 mg.;

1 0.000204 mole), and 1 ml. of glacial acetic acid are added.  
2 The mixture is stirred at reflux for 4 hours. Phosphorus  
3 is removed by filtration and washed with glacial acetic acid.  
4 The ice-cold filtrate is rendered strongly alkaline and the  
5 oily base that separates is extracted into benzene. Evapo-  
6 ration of the washed and dried benzene extract under  
7 reduced pressure leaves an oil. This residue is heated to  
8 refluxing for 1-1/2 hours in 1 ml. of 5% potassium hydroxide  
9 in 95% ethanol. The solvent is evaporated under reduced  
10 pressure and the residue partitioned between ether and water.  
11 The ethereal layer is separated, washed with water, dried  
12 by filtration through anhydrous magnesium sulfate, and  
13 evaporated under reduced pressure. The residual oily base,  
14 44 mg. (70%), is identical in infrared and proton magnetic  
15 resonance spectra to the compound prepared according to the  
16 previous example. Upon treatment with fumaric acid, the  
17 product is converted to the fumarate salt, m.p. 231-232°C.  
18 dec., that gives no depression in melting point on admixture  
19 with the fumarate of the compound prepared according to the  
20 previous example.

21                           Example 17

22 5-Acetyl-11-chloro-10,11-dihydro-5,10-methano-5H-dibenzo-  
23 [a,d]cycloheptene

24                         5-Acetyl-10,11-dihydro-5,10-methano-5H-dibenzo-  
25 [a,d]cyclohepten-11-ol (1.32 g., 0.005 molc) is added in  
26 portions to 5 ml. of thionyl chloride with stirring and  
27 cooling in an ice bath. After 4-1/2 hours of stirring at  
28 room temperature, the excess thionyl chloride is distilled  
29 under reduced pressure and at room temperature. The  
30 residual solid is suspended in absolute ethanol and the

1 concentrated hydrochloric acid (2 drops) is stirred and  
2 heated to refluxing in 1.6 ml. of nitrobenzene and 1.6 ml.  
3 of benzene for 20 minutes. During this period, the solids  
4 first form a ball and then a colorless, lower second phase.  
5 5-Acetyl-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cyclo-  
6 heptene (797 mg., 0.0032 mole) is added and the mixture is  
7 stirred at reflux for 2-1/2 hours. During the final 15  
8 minutes of this period, the condenser is removed so that  
9 water in the mixture may distill azeotropically. On cooling,  
10 the hydrochloride of the product precipitates and is collect-  
11 ed, washed with ether, and triturated with boiling isopropyl  
12 alcohol, m.p. 210-212°C. Recrystallization from mixtures  
13 of absolute ethanol and absolute ether affords an analytical  
14 sample, m.p. 211-213°C.

15                 Anal. calc'd. for  $C_{21}H_{23}NO \cdot HCl$ : C, 73.77; H, 7.07;  
16 N, 4.10. Found: C, 73.57; H, 6.94, N, 4.03.

17                 Example 20

18 1-(10,11-Dihydro-5,10-methano-5H-dibenzo[a,d]cyclohepten-5-yl)-  
19 3-dimethylamino-1-propanol

20                 1-(10,11-Dihydro-5,10-methano-5H-dibenzo[a,d]-  
21 cyclohepten-5-yl)-3-dimethylamino-1-propanone (376 mg.,  
22 0.00123 mole) is dissolved in 15 ml. of absolute methanol.  
23 A solution of potassium borohydride (135 mg., 0.0025 mole)  
24 in 1 ml. of water containing 1 drop of 5% aqueous sodium  
25 hydroxide is added and the mixture, after stirring at room  
26 temperature for 3 hours, is maintained at 0 - 5°C. for 2 days.  
27 Methanol is distilled under reduced pressure and the residue  
28 partitioned between benzene and water. Evaporation of the  
29 washed and dried benzene extract leaves the oily product  
30 in a yield of 317 mg. The base is converted to the fumarate

2 amount of fumaric acid dissolved in ethanol. 1-(10,11-  
3 Dihydro-5,10-methano-5H-dibenzo[a,d]cycloheptene-5-yl)-3-  
4 dimethylamino-1-propanol fumarate crystallizes, m.p. 228-230°C.  
5 and gives no depression in melting point on admixture with  
6 the product prepared according to the previous example.

7                   Example 21

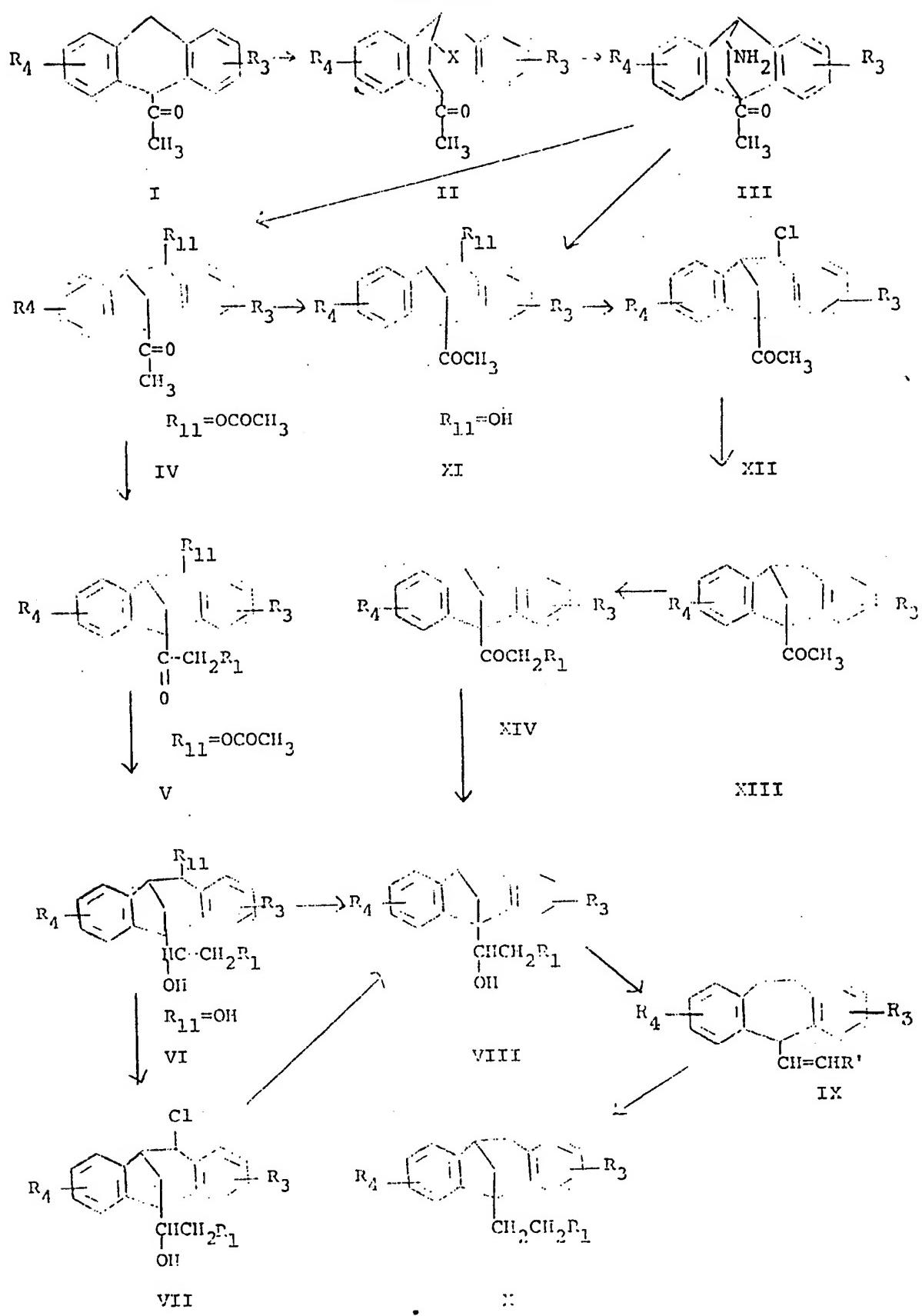
8 10,11-Dihydro-5-(1-chloro-3-dimethylaminopropyl)-5,10-methano-  
9 5H-dibenzo[a,d]cycloheptene and 1-(10,11-dihydro-5,10-methano-  
10 5H-dibenzo[a,d]cycloheptene-5-yl)-3-dimethylamino-1-propene

11                 1-(10,11-Dihydro-5,10-methano-5H-dibenzo[a,d]cyclo-  
12 hepten-5-yl)-3-dimethylamino-1-propanol, 399 mg. (0.0013 mole),  
13 is converted to the hydrochloride salt by treatment of a  
14 benzene solution with an excess amount of ethanolic hydrogen  
15 chloride. Evaporation of the solution under reduced pressure  
16 leaves the white solid hydrochloride which is dried in vacuo  
17 at 70°C. A suspension of the hydrochloride in 2 ml. of  
18 chloroform and 0.5 ml. of phosphorus oxychloride is stirred  
19 at reflux for 30 hours. A clear solution is obtained after  
20 2-3 hours. After cooling and dilution with chloroform, the  
21 mixture is extracted with ice-water. The chloroform layer is  
22 separated and evaporated to dryness leaving an oily residue  
23 which is triturated with cold dilute hydrochloric acid and  
24 filtered. The aqueous extracts are combined, rendered strongly  
25 alkaline with 5% aqueous sodium hydroxide, and the oily base  
26 extracted into 1:1 benzene:ether. Evaporation of the washed  
27 and dried organic extract under reduced pressure leaves a  
28 viscous oil containing a mixture of 10,11-dihydro-5-(1-  
29 chloro-3-dimethylaminopropyl)-5,10-methano-5H-dibenzo[a,d]-  
30 cycloheptene and 1-(10,11-dihydro-5,10-methano-5H-dibenzo-  
31 [a,d]cyclohepten-5-yl)-3-dimethylamino-1-propene. The  
32 hydrogen oxalate salt of this product is obtained by treating

1 charcoal catalyst. The product obtained in this manner is  
2 similarly separated from the catalyst and recrystallized  
3 from a mixture of isopropyl alcohol and water.

4 Various changes and modifications of the invention  
5 can be made, and to the extent that such variations incorpo-  
6 rate the spirit of this invention, they are intended to be  
7 included within the scope of the appended claims.

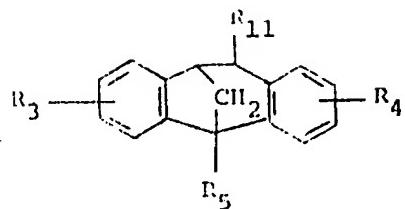
FLOW SHEET



now particularly described and ascertained my/our said invention and  
what manner the same is to be performed, I/we declare that what follows:

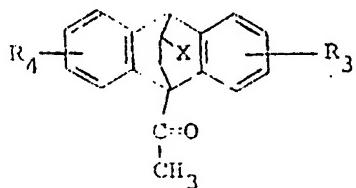
1. A compound selected from a 10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cycloheptene having a primary, secondary or tertiary aminoalkyl substituent at the 5-position or a 9-alkanoyl-9,10-ethanodihydroanthracene compound containing an amino, carboxy or esterified carboxy substituent attached to one of the carbons of the ethano bridge.
2. A compound in accordance with Claim 1 comprising a 10,11-dihydro-5,10-methano-5H-dibenzo[a,d]-cycloheptene compound substituted at the 5-position with a primary, secondary or tertiary aminoalkyl substituent.
3. A compound in accordance with Claim 1 comprising a 9-alkanoyl-9,10-ethanodihydroanthracene compound wherein one of the carbons of the ethano bridge is substituted with an amino, a carboxy or an esterified carboxy substituent.

4. A compound in accordance with Claim 1 having the structural formula



wherein R<sub>5</sub> is an aliphatic substituent substituted by one or more members selected from the group comprising ketonic oxygen, hydroxyl, amino, alkylamino, or dialkylamino; R<sub>3</sub> and R<sub>4</sub> are hydrogen, halo, alkyl, alkoxy, or trifluoromethyl, and R<sub>11</sub> is hydroxyl, alkanoyloxy.

5. A compound in accordance with Claim 1 having the structural formula



wherein R<sub>3</sub> and R<sub>4</sub> are hydrogen, halo, alkyl, alkoxy or trifluoromethyl and X is amino, carboxy or esterified carboxy.

6. A compound in accordance with Claim 5 consisting of 9-acetyl-9,10-dihydro-9,10-ethanoanthracene-11-carboxylic acid.

7. A compound in accordance with Claim 5 consisting of 9,10-dihydro-9-(2-methyl-1,3-dioxolan-2-yl)-9,10-ethanoanthracene-11-carboxylic acid.

8. A compound in accordance with Claim 5 consisting of methyl-9,10-dihydro-9-(2-methyl-1,3-dioxolan-2-yl)-9,10-ethanoanthracene-11-carboxylate.

9. A compound in accordance with Claim 5 consisting of methyl-9-acetyl-9,10-dihydro-9,10-ethanoanthracene-11-carboxylate.

10. A compound in accordance with Claim 5 consisting of methyl-9,10-dihydro-9-(2-methyl-1,3-dioxolan-2-yl)-9,10-ethanoanthracene-11-carboxylate.

11. A compound in accordance with Claim 5 consisting of 9,10-dihydro-9-(2-methyl-1,3-dioxolan-2-yl)-9,10-ethanoanthracene-11-carboxylic acid hydrazide.

12. A compound in accordance with Claim 5 consisting of 9,10-dihydro-11-ethoxycarbonylamino-9-(2-methyl-1,3-dioxolan-2-yl)-9,10-ethanoanthracene.

13. A compound in accordance with Claim 5 consisting of 9-acetyl-11-amino-9,10-dihydro-9,10-ethanoanthracene.

14. A compound according to Claim 4 consisting of 11-acetoxy-5-acetyl-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cycloheptene.

15. A compound according to Claim 4 consisting of 5-acetyl-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cyclohepten-11-ol.

16. A compound according to Claim 4 consisting of 1-(11-acetoxy-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]-cyclohepten-5-yl)-3-dimethylamino-1-propanone hydrochloride.

17. A compound according to Claim 4 consisting of 1-(10,11-dihydro-11-hydroxy-5,10-methano-5H-dibenzo-[a,d]cyclohepten-5-yl)-3-dimethylamino-1-propanol.

18. A compound according to Claim 4 consisting of 1-(11-chloro-10,11-dihydro-5,10-methano-5H-dibenzo-[a,d]cyclohepten-5-yl)-3-dimethylamino-1-propanol hydrochloride.

19. A compound according to Claim 4 consisting of 1-(10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cyclohepten-5-yl)-3-dimethylamino-1-propanol.

20. A compound according to Claim 4 consisting of 5-acetyl-11-chloro-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cycloheptene.

21. A compound according to Claim 4 consisting of 5-acetyl-10,11-dihydro-5,10-methano-5H-dibenzo[a,d]-cycloheptene.

22. A compound according to Claim 4 consisting of 1-(10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cyclohepten-5-yl)-3-dimethylamino-1-propanone.

23. The process for preparing a 10,11-dihydro-5,10-methano-5H-dibenzo[a,d]cycloheptene compound containing an alkylaminoalkyl substituent attached to the 5-position which comprises heating a 9-alkanoylanthracene in contact with acrylic acid or an ester thereof to form a 9-alkanoyl-9,10-ethano-11-carboxy or carbalkoxydihydroanthracene, subsequently reacting said carboxy or carbalkoxy compound with hydrazine to form the corresponding 9-alkanoyl-9,10-ethanodihydro-anthracene-11-carboxylic acid hydrazide, contacting said hydrazide with nitrous acid to form the corresponding 11-urethane and hydrolyzing said urethane to produce 9-alkanoyl-11-amino-9,10-dihydroanthracene, heating said 11-aminoanthracene compound in contact with nitrous acid to form a 5-alkanoyl-10,11-dihydro-5,10-methano-11-hydroxy or acyloxy-5H-dibenzo[a,d]cycloheptene, heating said cycloheptene compound in acid solution in contact with an amine and an aldehyde to form a 5-dialkylaminoalkanoyl-5,10-methano-10,11-dihydro-5H-dibenzo[a,d]cycloheptene, reducing said dialkylaminoalkanoyl cycloheptene compound by heating in contact with an alkali metal borohydride to produce the corresponding 5-(alkylamino-hydroxyalkyl)-5,10-methano-10,11-dihydro-5H-dibenzo[a,d]-cycloheptene, dehydrating said hydroxyalkyl cycloheptene compound to form the corresponding 5-alkylaminoalkenyl-5,10-methano-10,11-dihydro-5H-dibenzo[a,d]cycloheptene, and hydrogenating said alkenyl compound in the presence of a catalyst to produce the corresponding 5-alkylaminoalkyl-5,10-methano-10,11-dihydro-5H-dibenzo[a,d]cycloheptene.

5,10-methano-5H-dibenzo[a,d]cycloheptene compound containing an alkylaminoalkyl substituent attached to the 5-position which comprises heating a 9-alkanoylanthracene in contact with acrylic acid or an ester thereof to form a 9-alkanoyl-9,10-ethano-11-carboxy or carbalkoxydihydroanthracene.

25. The process which comprises heating a 9-alkanoyl-9,10-ethano-11-amino-9,10-dihydroanthracene compound in intimate contact with nitrous acid to form a 5-alkanoyl-10,11-dihydro-5,10-methano-11-hydroxy or acyloxy-5H-dibenzo[a,d]cycloheptene.

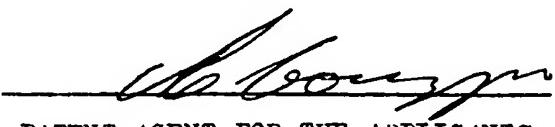
26. The process which comprises heating a 5-alkanoyl-10,11-dihydro-5,10-methano-11-hydroxy or acyloxy-5H-dibenzo[a,d]cycloheptene in contact with an amine and an aldehyde under acidic conditions to form a 5-dialkylamino-alkanoyl-5,10-methano-10,11-dihydro-5H-dibenzo[a,d]cycloheptene and reducing said dialkylaminoalkanoyl cycloheptene compound by heating in contact with an alkali metal borohydride to produce the corresponding 5,10-methano-10,11-dihydro-5H-dibenzo[a,d]cycloheptene compound having a radical derived from an alkylaminoalkanol attached to the 5-position.

27. Novel derivatives of dibenzocycloheptenes substantially as described herein with particular reference to the accompanying examples.

28. A process for the preparation of dibenzocycloheptenes substantially as described herein with particular reference to the accompanying examples.

29. The product when obtained by the process of any of the claims 23 to 26 and 28.

DATED this 20th day of March, 1968.

  
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PATENT AGENT FOR THE APPLICANTS.